

**附录 4：国外学者研究发现草甘膦是内分泌干扰剂 17 项科学试验证据！**

**Attachment 4: Seventeen studies show evidence that glyphosate is an Endocrine Disrupting Chemical (EDC).**

国外学者研究发现草甘膦是内分泌干扰剂 17 项科学试验证据。农业部与中国疾控中心沿用传统毒理学已经过时的“剂量决定毒性”错误观念，故意无视草甘膦等内分泌干扰剂这样的化学品在极低微量危害人类的一系列内分泌激素，对健康造成终生多方面系统性损害！

The Ministry of Agriculture and the China Disease Prevention & Control Center (China CDC) continue to use the out of date "dosage decides toxicity" concept of traditional toxicology, purposely ignoring that chemicals like glyphosate and other EDCs, at very low level cause harm to a series of hormone systems of humans, causing life-long systematic harm in many aspects!

### 要点概述

### **Summary of Main Points**

中国学者任晋、蒋可 2001 年《内分泌干扰剂的研究进展》摘要：内分泌干扰剂（EDC）正在成为生态环境研究的前沿课题，并受到各国政府的密切关注。本文综述了内分泌干扰剂的危害、作用机理、化合物类型及研究进展，特别强调了化合物低剂量长期暴露潜在危害的新概念，详述了传统的环境毒理学和环境分析化学所遇到的挑战及生物分析、化学仪器分析和生物传感器技术在内分泌干扰剂筛选过程中的重要战略地位。

**"Advances of Endocrine Disrupting Chemicals Research" by Chinese scholar Ren Jin, Jiang Ke, Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences.** Summary: EDC is becoming a front-edge topic of ecological environment studies, and receiving close attention by governments of each nation. This paper summarizes advances in the studies of the harms caused by EDCs, their mechanism, kinds of compounds, and especially emphasizes on the new concept of potential harm caused by low

concentrations but long-term exposure to such chemical compounds, discussed in detail the challenge traditional environment toxicology and environment analysis chemistry has faced, the important strategic position of biological analysis, chemical instrument analysis and biosensors technology in the screening process of EDCs.

**"Endocrine Disruptor Screening Program (EDSP)" issued on April15, 2009 by EPA points out:**

美国环境保护署（EPA）2009年4月15日《内分泌干扰剂筛选程序（EDSP）》指出：

**In the 1990's, some scientists proposed that certain chemicals might be disrupting the endocrine systems of humans and wildlife. A variety of chemicals have been found to disrupt the endocrine systems of animals in laboratory studies, and compelling evidence shows that endocrine systems of certain fish and wildlife have been affected by chemical contaminants, resulting in developmental and reproductive problems.**

90年代，某些科学家提议某些化学品可能对人类与野生动物内分泌系统造成干扰。在实验室研究总发现一系列化学品对动物内分泌系统造成干扰，令人信服的证据表明某些鱼类与野生动物的内分泌系统遭到化学污染的影响，导致发育与繁殖性问题。

**Based on this and other evidence, Congress passed the Food Quality Protection Act and the Safe Drinking Water Act (SDWA) Amendments in 1996 requiring that EPA screen pesticide chemicals for their potential to produce effects similar to those produced by the female hormones (estrogen) in humans and giving EPA the authority to screen certain other chemicals and to include other endocrine effects. Based on recommendations from an Advisory Committee, EPA has expanded the EDSP to include male hormones (androgens) and the thyroid system, and to include effects on fish and wildlife.**

基于此以及其他证据，国会1996年通过了《食品质量保护法》与《安全饮水法》修订案，要求环境保护署对于农药化学品产生雌性激素（雌激素）

在人类中造成同样影响的潜在可能进行筛选，并且授权环境保护署对某些其他的化学品，并包括其他内分泌影响，进行筛选。基于一个咨询委员会的推荐意见，环境保护署扩展了 EDSP（内分泌干扰剂筛选程序），将男性激素（雄激素）以及甲状腺系统包括进来，同时包括对鱼类与野生动物的影响。

"Environmental causes of cancer: endocrine disruptors as carcinogens" published in 2010 by *Nature Reviews Endocrinology* emphasizes:

《自然杂志》2010年《致癌环境性原因：致癌的内分泌干扰剂，自然内分泌腺审查》强调：

Environmental endocrine disrupting chemicals (EDCs), including pesticides and industrial chemicals, have been and are released into the environment producing deleterious effects on wildlife and humans. The effects observed in animal models after exposure during organogenesis correlate positively with an increased incidence of malformations of the male genital tract and of neoplasms and with the decreased sperm quality observed in European and US populations. Exposure to EDCs generates additional effects, such as alterations in male and female reproduction and changes in neuroendocrinology, behavior, metabolism and obesity, prostate cancer and thyroid and cardiovascular endocrinology. This Review highlights the carcinogenic properties of EDCs, with a special focus on bisphenol A. However, humans and wildlife are exposed to a mixture of EDCs that act contextually. To explain this mindboggling complexity will require the design of novel experimental approaches that integrate the effects of different doses of structurally different chemicals that act at different ages on different target tissues.

环境性内分泌干扰化学品（EDC），包括农药与工业化学品，释放到环境中对野生动物与人类造成有害影响。动物模型中观察到的接触内分泌干扰化学品后器官形成中发现的影响，与欧洲与美国人口中观察到的男性生殖系统及其赘生物与精子治疗降低的状况正向关联。接触环境性内分泌干扰化学品还产生其他的影响，例如男性与女性繁殖中的改变、神经内分泌、行为、新陈代谢与肥胖症、前列腺癌与甲状腺与心血管内分泌异常。

该审查汇集环境性内分泌干扰化学品的致癌性质，并特别关注双酚的作用。然而，人类与野生动物接触多种相互作用的环境性内分泌干扰化学品的混合体。为了解释这种极费脑筋的复杂状况，要求设计新的实验方法，综合考虑不同结构不同剂量不同化学品的作用，它们在不同的年龄段对不同靶标造成不同的影响。

**Vandenberg LN et al. (2012) reveals:** For decades, studies of endocrine-disrupting chemicals (EDCs) have challenged traditional concepts in toxicology, in particular the dogma of “the dose makes the poison,” because EDCs can have effects at low doses that are not predicted by effects at higher doses. Here, we review two major concepts in EDC studies: low dose and nonmonotonicity. ... We conclude that when nonmonotonic dose-response curves occur, the effects of low doses cannot be predicted by the effects observed at high doses. Thus, fundamental changes in chemical testing and safety determination are needed to protect human health.

**Vandenberg LN et al. (2012) 揭示：**传统毒理学一直坚持的法则。近几十年，内分泌干扰化学品（EDC）的研究对毒理学传统概念“剂量致毒性”的法则提出了挑战，因为内分泌干扰化学品（EDC）高剂量的影响无法预测低剂量的影响。我们审查了内分泌干扰化学品（EDC）研究中的两项主要概念：低剂量与非单调性（nonmonotonicity）。... 我们结论，非单调性剂量响应曲线发生时，低剂量时的效应无法由高剂量观察到的效应进行预测。因此，对毒理学中化学测试与毒性确定需要做实质性改变来保护人类安全。

**The EPA on April 14, 2009 announced the preliminary list for the Endocrine Disruptor Screening Program, which included glyphosate.**

环境保护署 2009 年 4 月 14 日宣布了对内分泌系统潜在影响进行筛选的化学品初步清单，其中包括草甘膦。

国外学者研究发现草甘膦是内分泌干扰剂 17 项科学试验证据！

**Oversea 17 studies find evidence that glyphosate is an EDC!**

**1) Yousef MI et al. (1995):** Pesticide treatment resulted in a decline in body weight, libido, ejaculate volume, sperm concentration, semen initial fructose and semen osmolality. This was accompanied with increases in the abnormal and dead sperm and semen methylene blue reduction time. The hazardous effect of these pesticides on semen quality continued during the recovery period, and was dose-dependent. These effects on sperm quality may be due to the direct cytotoxic effects of these pesticides on spermatogenesis and/or indirectly via hypothalami-pituitary-testis axis which control the reproductive efficiency.

**1) Yousef MI et al. (1995):** 草甘膦造成实验兔体重、性欲、射精量、精子浓度等指标下降，危害精子质量的作用终止处理后继续发展，而且剂量依赖。机理可能是草甘膦对精子声称的直接细胞毒性，和/或间接通过控制繁殖效率的视丘下部垂体睾丸轴造成这些损害。

**2) Walsh, L.P. et al. (2000):** The pesticide Roundup inhibited dibutyryl [(Bu)<sub>2</sub>]cAMP-stimulated progesterone production in MA-10 cells without causing cellular toxicity. Roundup inhibited steroidogenesis by disrupting StAR protein expression, further demonstrating the susceptibility of StAR to environmental pollutants.

**2) Walsh, L.P. et al. (2000):** 在小鼠肿瘤细胞中发现草甘膦除草剂农达抑制参与性激素蛋白质生物合成活动。这把胆固醇 -- 妊娠烯醇酮 -- 孕激素转换途径的运行降低到最低水平。

**3) Marc J et al. (2002):** In summary, Roundup affects cell cycle regulation by delaying activation of the CDK1/cyclin B complex, by synergic effect of glyphosate and formulation products. Considering the universality among species of the CDK1/cyclin B regulator, our results question the safety of glyphosate and Roundup on human health.

**3) Marc J et al. (2002):** 简要讲，农达通过草甘膦及其配方制剂的协同效应延迟 CDK1/细胞周期蛋白 B 的活动性影响细胞的生长周期。考虑到不

同物种中 CDK1/细胞周期蛋白 B 调制器的普遍性，我们质疑草甘膦与农达对人类健康的安全性。

**4) Marc, J et al. (2004):** At a concentration that efficiently impeded the cell cycle, formulated glyphosate inhibited the synthesis of DNA occurring in S phase of the cell cycle. The extent of the inhibition of DNA synthesis by formulated glyphosate was correlated with the effect on the cell cycle. We conclude that formulated glyphosate's effect on the cell cycle is exerted at the level of the DNA-response checkpoint of S phase. The resulting inhibition of CDK1/cyclin B Tyr 15 dephosphorylation leads to prevention of the G2/M transition and cell cycle progression.

**4) Marc, J et al. (2004):** 草甘膦除草剂抑制首个细胞周期的 G2/M 阶段的 DNA 生物合成。

**5) Marc, J et al. (2004):** Roundup Biovert induced cell cycle dysfunction. The threshold concentration for induction of cell cycle dysfunction was evaluated for each product and suggests high risk by inhalation for people in the vicinity of the pesticide handling sprayed at 500 to 4000 times higher dose than the cell-cycle adverse concentration.

**5) Marc, J et al. (2004) :** 农业喷洒剂量稀释 500 至 4000 倍的草甘膦除草剂导致发展癌症的细胞周期机能失调。

**6) Beuret CJ et al (2005):** The present study has investigated the effects that 1% glyphosate oral exposure has on lipoperoxidation and antioxidant enzyme systems in the maternal serum and liver of pregnant rats and their term fetuses at 21 days of gestation. The results suggest that excessive lipid peroxidation induced with glyphosate ingestion leads to an overload of maternal and fetal antioxidant defense systems.

**6) Beuret CJ et al (2005):** 研究试验口服 1% 浓度草甘膦在 21 天孕期中对怀孕鼠的血清与肝及其胎儿的脂质过氧化与抗氧化酶系统的影响。结果

发现，摄入草甘膦诱发过量脂质过氧化，导致对怀孕鼠及其胎儿抗氧化防御系统过量。

7) **Richard S et al. (2005)**: We tested the effects of glyphosate and Roundup at lower nontoxic concentrations on aromatase, the enzyme responsible for estrogen synthesis. The glyphosate-based herbicide disrupts aromatase activity and mRNA levels and interacts with the active site of the purified enzyme, but the effects of glyphosate are facilitated by the Roundup formulation in microsomes or in cell culture. We conclude that endocrine and toxic effects of Roundup, not just glyphosate, can be observed in mammals. We suggest that the presence of Roundup adjuvants enhances glyphosate bioavailability and/or bioaccumulation.

7) **Richard S et al. (2005)** 在哺乳动物中可以观察到草甘膦除草剂农达的内分泌干扰与毒性影响，不仅是草甘膦的内分泌干扰与毒性影响。我们认为农达的辅佐剂强化了的草甘膦的生物可获得性和/或生物积蓄。

8) **Oliveira AG et al. (2007)**: The exposure to the herbicide resulted in alterations in the structure of the testis and epididymal region as well as in the serum levels of testosterone and estradiol, with changes in the expression of androgen receptors restricted to the testis. The harmful effects were more conspicuous in the proximal efferent ductules and epididymal ducts, suggesting higher sensitivity of these segments among the male genital organs. The effects were mostly dose dependent, indicating that this herbicide may cause disorder in the morphophysiology of the male genital system of animals.

8) **Oliveira AG et al. (2007)**: 接触草甘膦除草剂造成对睾丸与附睾区域构造的改变，还改不了血清中睾丸激素与雌二醇的水平，改变了睾丸雄性激素受体的表达。更明显的近端传对微胆管和附睾导管造成有害影响，表明雄生殖器中这些部位对草甘膦更为敏感。造成的影响具有剂量依赖性，表明草甘膦除草剂可能在动物雄生殖系统中造成形态生理学失调。

**9) Dallegrave E et al. (2007):** The results showed that glyphosate-Roundup did not induce maternal toxicity but induced adverse reproductive effects on male offspring rats: a decrease in sperm number per epididymis tail and in daily sperm production during adulthood, an increase in the percentage of abnormal sperms and a dose-related decrease in the serum testosterone level at puberty, and signs of individual spermatid degeneration during both periods. There was only a vaginal canal-opening delay in the exposed female offspring. These findings suggest that in utero and lactational exposure to glyphosate-Roundup may induce significant adverse effects on the reproductive system of male Wistar rats at puberty and during adulthood.

**9) Dallegrave E et al. (2007) :** 研究结果表明，草甘膦除草剂农达没有诱发雌鼠毒性，但是对雄性后代造成了有害繁殖性影响：鼠仔成年后每个附睾精子数量与每天精子产生量减少、增加异常精子百分比，进入青春期后血清睾丸激素水平产生与草甘膦接触量相关减少，同时在两个阶段出现精子退化迹象。后代雌鼠仔长大后仅发生阴道开通延迟。这些发现表明，子宫内与哺乳期接触草甘膦除草剂农达可能对雄鼠仔进入青春期与成年期阶段的生殖系统诱发显著有害影响。

**10) Nora Benachour et al. (2009):** We have evaluated the toxicity of four glyphosate (G)-based herbicides in Roundup (R) formulations, from 105 times dilutions, on three different human cell types. This dilution level is far below agricultural recommendations and corresponds to low levels of residues in food or feed. The formulations have been compared to G alone and with its main metabolite AMPA or with one known adjuvant of R formulations, POEA. HUVEC primary neonate umbilical cord vein cells have been tested with 293 embryonic kidney and JEG3 placental cell lines. All R formulations cause total cell death within 24 h, through an inhibition of the mitochondrial succinate dehydrogenase activity, and necrosis, by release of cytosolic adenylate kinase measuring membrane damage. They also induce apoptosis via activation of

enzymatic caspases 3/7 activity. This is confirmed by characteristic DNA fragmentation, nuclear shrinkage (pyknosis), and nuclear fragmentation (karyorrhexis), which is demonstrated by DAPI in apoptotic round cells. G provokes only apoptosis, and HUVEC are 100 times more sensitive overall at this level. The deleterious effects are not proportional to G concentrations but rather depend on the nature of the adjuvants. AMPA and POEA separately and synergistically damage cell membranes like R but at different concentrations. Their mixtures are generally even more harmful with G. In conclusion, the R adjuvants like POEA change human cell permeability and amplify toxicity induced already by G, through apoptosis and necrosis. The real threshold of G toxicity must take into account the presence of adjuvants but also G metabolism and time-amplified effects or bioaccumulation. This should be discussed when analyzing the *in vivo* toxic actions of R. This work clearly confirms that the adjuvants in Roundup formulations are not inert. Moreover, the proprietary mixtures available on the market could cause cell damage and even death around residual levels to be expected, especially in food and feed derived from R formulation-treated crops.

10) Nora Benachour et al. (2009) :对草甘膦及其主要代谢物 AMPA，以及草甘膦添加除草剂配方中主要辅佐剂 POEA(表面活性剂, 稀释 10 万倍，对三种不同的人类细胞的毒性。这样的稀释水平，远远低于农业应用推荐的水平，并对应于食品或者饲料中草甘膦残留的低水平。三种人类细胞分别为新生儿脐带静脉的细胞、293 胚肾细胞与 JEG3 胎盘细胞系。所有草甘膦的配方在 24 小时内造成所有细胞死亡，通过抑制线粒体琥珀酸脱氢酶活性，以及通过释放胞质膜伤害腺苷酸激酶测量膜损伤导致坏疽。通过激活酶的半胱天冬酶 3/7 活性诱发细胞凋亡。单独草甘膦激起仅细胞凋亡，而人脐静脉内皮细胞 (HUVEC) 在这个水平上 100 倍更敏感。有害效应与草甘膦浓度不成比例，更加取决于除草剂辅佐剂的性质。草甘膦代谢物 AMPA 与 POEA (草甘膦除草剂配方中的表面活性剂)，分别单独作用或者合在一起协作用时，像草甘膦一样，损伤细胞膜，但是各自在不同的浓度发挥作用。它们与草甘膦一起的混合物的危害通常更强。结论，像 POEA

这样的辅佐剂，改变人类细胞的渗透性，以凋亡与坏疽方式强化诱发草甘膦诱发的毒性。草甘膦真正的阈值，必须考虑存在的辅佐剂，还必须考虑草甘膦的代谢、时间放大效应或生物蓄积作用。市场上销售的草甘膦除草剂，即便在抗草甘膦作物加工的食品与饲料残留水平，能够造成细胞损伤以至死亡。

**11) Gasnier C et al. (2009):** Glyphosate-based herbicides are the most widely used across the world; they are commercialized in different formulations. Their residues are frequent pollutants in the environment. In addition, these herbicides are spread on most eaten transgenic plants, modified to tolerate high levels of these compounds in their cells. Up to 400 ppm of their residues are accepted in some feed. We exposed human liver HepG2 cells, a well-known model to study xenobiotic toxicity, to four different formulations and to glyphosate, which is usually tested alone in chronic in vivo regulatory studies. We measured cytotoxicity with three assays (Alamar Blue, MTT, ToxiLight), plus genotoxicity (comet assay), anti-estrogenic (on ERalpha, ERbeta) and anti-androgenic effects (on AR) using gene reporter tests. We also checked androgen to estrogen conversion by aromatase activity and mRNA. All parameters were disrupted at sub-agricultural doses with all formulations within 24h. These effects were more dependent on the formulation than on the glyphosate concentration. First, we observed a human cell endocrine disruption from 0.5 ppm on the androgen receptor in MDA-MB453-kb2 cells for the most active formulation (R400), then from 2 ppm the transcriptional activities on both estrogen receptors were also inhibited on HepG2. Aromatase transcription and activity were disrupted from 10 ppm. Cytotoxic effects started at 10 ppm with Alamar Blue assay (the most sensitive), and DNA damages at 5 ppm. A real cell impact of glyphosate-based herbicides residues in food, feed or in the environment has thus to be considered, and their classifications as carcinogens/mutagens/reprotoxics is discussed.

**11) Gasnier C et al. (2009) :草甘膦为基础草甘膦在世界上最广泛使用。**

它们的残留成为环境中经常有的污染物。此外，这些除草剂还喷洒到最大量食用的转基因作物，这样的作物使其容忍细胞中高水平的这些成分。某些饲料中允许它们高达 400 ppm 残留。人类肝脏 HepG2 细胞是研究异型生物质毒性的知名模型，我们让人类肝脏 HepG2 细胞接触草甘膦及其四种不同配方除草剂制剂。通常仅在慢性活体内对单独草甘膦成分进行试验。我们用三种试验方法 (Alamar Blue, MTT, ToxiLight)，以及基因毒性 (彗星试验)、抗雌激素 (对 ERalpha, ERbeta) 与抗雄激素效果 (对 AR) 做基因检测试验。我们还用芳香化酶活性与 mRNA 检测雄激素雌激素转换。所有指标在 24 小时内都受到亚农业用剂量用的草甘膦及其四种配方除草剂制剂所有成分的干扰。其效果更依赖于草甘膦除草剂的配方而非草甘膦的剂量。首先观察到的人类细胞内分泌干扰是最为活性配方制剂 (R400) 从 0.5 ppm 剂量在 MDA-MB453-kb2 细胞中对雄激素受体的作用，然后从 2 ppm 剂量起，HepG2 细胞的两个雌激素受体的转录活动性遭到抑制。从 10 ppm 剂量起，芳香化酶转录和活动收到干扰。在 Alamar Blue 试验 (最敏感的) 中，从 10 ppm 剂量其发生细胞毒性作用，但从 5 ppm 起发生 DNA 损伤。因此必须考虑食物、饲料或者环境中草甘膦除草剂对真实细胞的影响，对草甘膦分类为致癌物/致突变/致生殖毒性进行了讨论。

12) Romano RM et al. (2010): These results suggest that commercial formulation of glyphosate is a potent endocrine disruptor in vivo, causing disturbances in the reproductive development of rats when the exposure was performed during the puberty period.

12) Romano RM et al. (2010) :研究结果表明商业配方的草甘膦除草剂在体内是一种威力强大的内分泌干扰剂，青春期接触时对老鼠的生育系统发育造成干扰。

13) Jayawardene, U.A et al.(2010): Glyphosate recorded the highest percentage of malformation (69%) compared to other pesticides in 1.00 ppm concentration. Malformations observed were mainly in the spine, such as hunched back (kyphosis) and curvature (scoliosis), while edema and skin ulcers

were also observed

**13)** Jayawardene, U.A et al. (2010) :用 1ppm 浓度，草甘膦对沙漏树蛙蝌蚪处理后，造成几种农药中最高的 69% 畸形率。观察到的畸形主要为脊柱畸形，如驼背（驼背）和曲率（脊柱侧弯），也观察到而水肿和皮肤溃疡。

39) (2010):

**14)** Paganelli, A.et al. (2010): *Xenopus laevis* embryos were incubated with 1/5000 dilutions of a commercial GBH. The treated embryos were highly abnormal with marked alterations in cephalic and neural crest development and shortening of the anterior-posterior (A-P) axis. Alterations on neural crest markers were later correlated with deformities in the cranial cartilages at tadpole stages. Embryos injected with pure glyphosate showed very similar phenotypes. Moreover, GBH produced similar effects in chicken embryos, showing a gradual loss of rhombomere domains, reduction of the optic vesicles, and microcephaly. This suggests that glyphosate itself was responsible for the phenotypes observed, rather than a surfactant or other component of the commercial formulation. A reporter gene assay revealed that GBH treatment increased endogenous retinoic acid (RA) activity in *Xenopus* embryos and cotreatment with a RA antagonist rescued the teratogenic effects of the GBH. Therefore, we conclude that the phenotypes produced by GBH are mainly a consequence of the increase of endogenous retinoid activity.

**14)** Paganelli, A.et al. (2010) :非洲爪蟾蜍晶胚与稀释 5000 倍草甘膦除草剂一起孵化。经处理的晶胚高度异常，头盖与神经嵴明显改变，前后轴缩短。改变后神经嵴标记与颅软骨蝌蚪阶段畸形一致。注射单独草甘膦显示非常类似的畸形。草甘膦除草剂在鸡晶胚中显示类似的影响，显示一个逐渐失去了菱域。减少视觉囊泡和小头畸形。这表明草甘膦自己对观察到的畸形负责，而不是草甘膦除草剂配方中的表面活性剂或其他组分。一个报告基因分析，揭示草甘膦除草剂处理增加了非洲爪蟾蜍晶胚中的视黄酸活性，而且与 RA 拮抗剂的协作处理保持了草甘膦除草剂的致畸效应。因此结论草甘膦除草剂产生的显型主要是内源性类活动增加的结果。

**15)** Koller VJ (2012): Comparisons with results of earlier studies with lymphocytes and cells from internal organs indicate that epithelial cells are more susceptible to the cytotoxic and DNA-damaging properties of the herbicide and its formulation. Since we found genotoxic effects after short exposure to concentrations that correspond to a 450-fold dilution of spraying used in agriculture, our findings indicate that inhalation may cause DNA damage in exposed individuals.

**15)** Koller VJ (2012) :与早期的草甘膦对内部器官淋巴与细胞的研究进行比较表明，上皮细胞更容易受到细胞毒性，而且 DNA 损伤的性质与除草剂及其配方相关。由于我们发现农业中喷洒剂量稀释 450 倍的短期暴露造成基因毒性的影响，我们的发现表明，喷洒草甘膦除草剂可能造成吸入人类 DNA 损伤。

**16)** R. Mesnagea (2013): Among them, POE-15 clearly appears to be the most toxic principle against human cells, even if others are not excluded. It begins to be active with negative dose-dependent effects on cellular respiration and membrane integrity between 1 and 3 ppm, at environmental/occupational doses. We demonstrate in addition that POE-15 induces necrosis when its first micellization process occurs, by contrast to glyphosate which is known to promote endocrine disrupting effects after entering cells.

**16)** R. Mesnagea (2013): 在它们之中，(农达配方中的表面活性剂)**POE-15** 清楚显示是对人类细胞最为毒性的成分，即便不排除其他成分。他始于环境性/职业接触剂量 **1 - 3 ppm** 之间对细胞呼吸与细胞膜整体性负面的剂量依赖作用。我们演示了 **POE-15** 还在它的首次胶束化作用发生时诱发坏疽，这与草甘膦进入细胞后促进内分泌干扰作用有所不同。

**17)** Thongprakaisang S (2013): Glyphosate is an active ingredient of the most widely used herbicide and it is believed to be less toxic than other pesticides. However, several recent studies showed its potential adverse health effects to

humans as it may be an endocrine disruptor. This study focuses on the effects of pure glyphosate on estrogen receptors (ERs) mediated transcriptional activity and their expressions. Glyphosate exerted proliferative effects only in human hormone-dependent breast cancer, T47D cells, but not in hormone-independent breast cancer, MDA-MB231 cells, at  $10^{-12}$  to  $10^{-6}$  M in estrogen withdrawal condition. The proliferative concentrations of glyphosate that induced the activation of estrogen response element (ERE) transcription activity were 5-13 fold of control in T47D-KBluc cells and this activation was inhibited by an estrogen antagonist, ICI 182780, indicating that the estrogenic activity of glyphosate was mediated via ERs. Furthermore, glyphosate also altered both ER $\alpha$  and  $\beta$  expression. These results indicated that low and environmentally relevant concentrations of glyphosate possessed estrogenic activity. Glyphosate-based herbicides are widely used for soybean cultivation, and our results also found that there was an additive estrogenic effect between glyphosate and genistein, a phytoestrogen in soybeans. However, these additive effects of glyphosate contamination in soybeans need further animal study.

17) Thongprakaisang S (2013): 草甘膦是最为广泛使用并被人们相信比其他农药毒性较低的除草剂的活性成分。然而，最近几项研究显示它对人类潜在危害健康，而且可能是一种内分泌干扰剂。该项研究集中于纯草甘膦对雌激素受体蛋白（estrogen receptors）促进的转录活动性及其表达。草甘膦，在  $10^{-12}$  至  $10^{-6}$  M (万亿分之一至百万分之一质量) 范围，在雌激素撤走状态下仅对人类激素-依赖乳房癌细胞 T47D 细胞发挥增殖作用，而对激素-独立乳房癌细胞 MDA-MB231 细胞系没有这种作用。诱发 ERE(雌激素反应元素) 转录活动性达到 T47D-KBluc 细胞中对照组的 5-13 倍的产生增殖作用剂量的草甘膦，受到一种雌激素对抗药 ICI 182780 的抑制，表明草甘膦的雌激素活动性通过雌激素受体蛋白（estrogen receptors）发挥作用。此外，草甘膦既改变雌激素受体蛋白（estrogen receptors） $\alpha$ ，有改变其  $\beta$  表达。这些结果显示，在低的与环境性相关浓度下，草甘膦具有雌激素性活动。草甘膦为基础的除草剂广泛用于（转基因）大豆种植，而我们的结果发现，存在着草甘膦与大豆中的一种植物雌激素染料木黄酮

(genistein) 之间的额外雌激素作用。然而，草甘膦对于（转基因）大豆的这种额外的作用需要进行进一步的动物试验。

任晋、蒋可，内分泌干扰剂的研究进展，化学进展，2001, 13(2)

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[http://d.wanfangdata.com.cn/Periodical\\_hxjz200102009.aspx](http://d.wanfangdata.com.cn/Periodical_hxjz200102009.aspx)

**摘要：**内分泌干扰剂（EDC）正在成为生态环境研究的前沿课题，并受到各国政府的密切关注。本文综述了内分泌干扰剂的危害、作用机理、化合物类型及研究进展，特别强调了化合物低剂量长期暴露潜在危害的新概念，详述了传统的环境毒理学和环境分析化学所遇到的挑战及生物分析、化学仪器分析和生物传感器技术在内分泌干扰剂筛选过程中的重要战略地位。

美国环境保护署：内分泌干扰剂筛选程序（EDSP） – 2009 年 4 月 15 日

**U.S. Environmental Protection Agency: Endocrine Disruptor Screening Program (EDSP) -- April 15, 2009**

<http://www.epa.gov/endo/>

90 年代，某些科学家提议某些化学品可能对人类与野生动物内分泌系统造成干扰。在实验室研究总发现一系列化学品对动物内分泌系统造成干扰，令人信服的证据表明某些鱼类与野生动物的内分泌系统遭到化学污染的影响，导致发育与繁殖性问题。基于此以及其他的数据，国会 1996 年通过了《食品质量保护法》与《安全饮水法》修订案，要求环境保护署对于农药化学品产生雌性激素（雌激素）在人类中造成同样影响的潜在可能进行筛选，并且授权环境保护署对某些其他的化学品，并包括其他内分泌影响，进行筛选。基于一个咨询委员会的推荐意见，环境保护署扩展了 EDSP（内分泌干扰剂筛选程序），将男性激素（雄激素）以及甲状腺系统包括进来，同时包括对鱼类与野生动物的影响。

环境保护署 2009 年 4 月 14 日宣布了对内分泌系统潜在影响进行筛选的化学品初步清单（或第一层次试验），并且于 2009 年 10 月 29 日发布了第一批试验指令。试验指令是要求提供数据。现在，筛选正在进行，环境保护署正在对试验指应回应进行审查，并且正在对有关状态或试验指令回

应和/或有关试验要求的任何决定做出允许了解的安排。

## 《自然杂志》致癌环境性原因：致癌的内分泌干扰剂，自然内分泌腺审查， 2010

Ana M. Soto & Carlos Sonnenschein, Environmental causes of cancer: endocrine disruptors as carcinogens, *Nature Reviews Endocrinology* **6**, 363–370 (1 July 2010)

<http://www.nature.com/nrendo/journal/v6/n7/authors/nrendo.2010.87.html>

环境性内分泌干扰化学品（EDC），包括农药与工业化学品，释放到环境中对野生动物与人类造成有害影响。动物模型中观察到的接触内分泌干扰化学品后器官形成中发现的影响，与欧洲与美国人口中观察到的男性生殖系统及其赘生物与精子治疗降低的状况正向关联。接触环境性内分泌干扰化学品还产生其他的影响，例如男性与女性繁殖中的改变、神经内分泌、行为、新陈代谢与肥胖症、前列腺癌与甲状腺与心血管内分泌异常。该审查汇集环境性内分泌干扰化学品的致癌性质，并特别关注双酚的作用。然而，人类与野生动物接触多种相互作用的环境性内分泌干扰化学品的混合体。为了解释这种极费脑筋的复杂状况，要求设计新的实验方法，综合考虑不同结构不同剂量不同化学品的作用，它们在不同的年龄段对不同靶标造成不同的影响。

（2012）：传统毒理学一直坚持的法则。近几十年，内分泌干扰化学品（EDC）的研究对毒理学传统概念“剂量致毒性”的法则提出了挑战，因为内分泌干扰化学品（EDC）高剂量的影响无法预测低剂量的影响。我们审查了内分泌干扰化学品（EDC）研究中的两项主要概念：低剂量与非单调性（nonmonotonicity）。… 我们结论，非单调性剂量响应曲线发生时，低剂量时的效应无法由高剂量观察到的效应进行预测。因此，对毒理学中化学测试与毒性确定需要做实质性改变来保护人类安全。

Vandenberg LN, Colborn T, Hayes TB, et al. Hormones and endocrine-disrupting chemicals: Low-dose effects and nonmonotonic dose responses. *Endocr Rev.* 2012;33(3):378-455. doi:10.1210/er.2011-1050.  
Vandenberg LN, Colborn T, Hayes TB, et al. 激素与内分泌干扰化学品：低剂量效应与非单调性剂量响应。*内分泌审视。* 2012;33(3):378-455.  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3365860/>

**美国环境保护署：2009年4月进行第一层次筛选化学品的最终清单：包括草甘膦！**

**U.S. EPA: April 2009 Final List of Chemicals for Initial Tier 1 Screening: Glyphosate**

<http://www.epa.gov/endo/pubs/prioritysetting/finallist.html>

**科学证据1（1995）：**草甘膦造成实验兔体重、性欲、射精量、精子浓度等指标下降，危害精子质量的作用终止处理后继续发展，而且剂量依赖。机理可能是草甘膦对精子声称的直接细胞毒性，和/或间接通过控制繁殖效率的视丘下部垂体睾丸轴造成这些损害。

1) Yousef MI et al., Toxic effects of carbofuran and glyphosate on semen characteristics in rabbits. *J Environ Sci Health B.* 1995 Jul;30(4):513-34.  
Yousef MI et al., 呋喃丹与草甘膦对兔子精子特征的毒性影响，*环境科学健康学报。* 1995年7月，30(4):513-34.

就职机构：埃及亚历山大大学环境研究系

<http://www.ncbi.nlm.nih.gov/pubmed/7797819>

**科学证据2（2000年）：**在小鼠肿瘤细胞中发现草甘膦除草剂农达抑制参与性激素蛋白质生物合成活动。这把胆固醇 -- 妊娠烯醇酮 -- 孕激素转换途径的运行降低到最低水平。

2) Walsh, L.P. et al., (2000). Roundup inhibits steroidogenesis by disrupting

steroidogenic acute regulatory (StAR) protein expression. Environmental Health Perspectives, 108, 769-776.

Walsh, L.P. et al. (2000). 草甘膦除草剂农达通过干扰类固醇激素合成急性调节抑制(StAR)类固醇生成。环境健康前景, 108, 769-776.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1638308/>

**科学证据 3 (2002):** 简要讲, 农达通过草甘膦及其配方制剂的协同效应延迟 CDK1/细胞周期蛋白 B 的活动性影响细胞的生长周期。考虑到不同物种中 CDK1/细胞周期蛋白 B 调制器的普遍性, 我们质疑草甘膦与农达对人类健康的安全性。

3) Marc J, Mulner-Lorillon O, Boulben S, Hureau D, Durand G, Bellé R. Pesticide Roundup provokes cell division dysfunction at the level of CDK1/cyclin B activation. Chem Res Toxicol. 2002;15(3):326-31.

<http://www.ncbi.nlm.nih.gov/pubmed/11896679>

**科学证据 4 (2004 年):** 草甘膦除草剂抑制首个细胞周期的 G2/M 阶段的 DNA 生物合成。研究者们估计, 草甘膦生产厂的工人吸入该项试验中浓度 500-5000 倍浓度的草甘膦。

4) Marc, J et al., (2004). Formulated glyphosate activities the DNA-response checkpoint of the cell cycle leading to the prevention of G2/M transition. Toxicological Sciences, 82, 436-442.

Marc, J et al., (2004)。草甘膦基配方除草剂激化细胞周期的 DNA 反应检查点导致阻止 G2/M 转变。毒理性科学, 82, 436-442.

就职机构: 细胞周期发展生物站、国家科学研究所、法国皮尔与玛丽居里大学

<http://www.ncbi.nlm.nih.gov/pubmed/15375296>

**科学证据 5 (2004) :** 农业喷洒剂量稀释 500 至 4000 倍的草甘膦除草剂导致发展癌症的细胞周期机能失调。

5) Marc J1, Mulner-Lorillon O, Bellé R. Glyphosate-based pesticides affect cell cycle regulation. Biol Cell. 2004 Apr;96(3):245-9.

<http://www.ncbi.nlm.nih.gov/pubmed/15182708>

**科学证据 6 (2005) :** 研究试验口服 1% 浓度草甘膦在 21 天孕期中对怀孕鼠的血清与肝及其胎儿的脂质过氧化与抗氧化酶系统的影响。结果发现，摄入草甘膦诱发过量脂质过氧化，导致对怀孕鼠及其胎儿抗氧化防御系统过量。

6) Beuret CJ et al, Effect of the herbicide glyphosate on liver lipoperoxidation in pregnant rats and their fetuses.

Reprod Toxicol. 2005 Mar-Apr;19(4):501-4.

Beuret CJ et al, 草甘膦除草剂在怀孕鼠及其胎儿中对肝脂质过氧化的影响。繁殖毒理学杂志。2005 年 3 月 -4 月； 19(4):501-4.

就职机构：阿根廷国立圣路易斯大学生物学与药理学系

<http://www.ncbi.nlm.nih.gov/pubmed/15749264>

**科学证据 7 (2005) :** 在哺乳动物中可以观察到草甘膦除草剂农达的内分泌干扰与毒性影响，不仅是草甘膦的内分泌干扰与毒性影响。我们认为农达的辅佐剂强化了的草甘膦的生物可获得性和/或生物积蓄。

7) Richard S et al., Differential effects of glyphosate and roundup on human placental cells and aromatase. Environ Health Perspect. 2005 Jun;113(6):716-20.

Richard S et al., 草甘膦与草甘膦除草剂浓度对人类胎盘细胞与芳香酶的差异性影响。环境性健康前景。2005 年 6 月； 113(6):716-20.

就职机构：法国卡昂大学分子生物与生物化学实验室

<http://www.ncbi.nlm.nih.gov/pubmed/15929894>

科学证据 8 (2007)：接触草甘膦除草剂造成对睾丸与附睾区域构造的改变，还改不了血清中睾丸激素与雌二醇的水平，改变了睾丸雄性激素受体的表达。更明显的近端传对微胆管和附睾导管造成有害影响，表明雄生殖器中这些部位对草甘膦更为敏感。造成的影响具有剂量依赖性，表明草甘膦除草剂可能在动物雄生殖系统中造成形态生理学失调。

8) Oliveira AG et al., Effects of the herbicide Roundup on the epididymal region of drakes *Anas platyrhynchos*. *Reprod Toxicol*. 2007 Feb;23(2):182-91. Epub 2006 Nov 11.

Oliveira AG et al., 草甘膦除草剂农达对绿头鸭附睾部位的影响。繁殖毒理学。2007 年 2 月； 23(2):182-91。网络发表：2006 年 11 月 11 日。

就职机构：巴西 Minas Gerais 联邦大学形态学系

<http://www.ncbi.nlm.nih.gov/pubmed/17166697>

科学证据 9 (2007)：研究结果表明，草甘膦除草剂农达没有诱发雌鼠毒性，但是对雄性后代造成了有害繁殖性影响：鼠仔成年后每个附睾精子数量与每天精子产生量减少、增加异常精子百分比，进入青春期后血清睾丸激素水平产生与草甘膦接触量相关减少，同时在两个阶段出现精子退化迹象。后代雌鼠仔长大后仅发生阴道开通延迟。这些发现表明，子宫内与哺乳期接触草甘膦除草剂农达可能对雄鼠仔进入青春期与成年期阶段的生殖系统诱发显著有害影响。

9) Dallegrave E et al., Pre- and postnatal toxicity of the commercial glyphosate formulation in Wistar rats. *Arch Toxicol*. 2007 Sep;81(9):665-73. Epub 2007 Jul 19.

Dallegrave E et al.商业草甘膦除草剂配方在 Wistar 鼠中的出生前与出生后毒性，毒理学档案。2007 年 9 月； 81(9):665-73. 网络出版：2007 年 7 月 19 日。

就职机构：巴西 Rio Grande do Sul 联邦大学，药理学系  
<http://www.ncbi.nlm.nih.gov/pubmed/17634926>

**科学证据 10（2009）：**对草甘膦及其主要代谢物 AMPA，以及草甘膦添加除草剂配方中主要辅佐剂 POEA（表面活性剂，稀释 10 万倍，对三种不同的人类细胞的毒性。这样的稀释水平，远远低于农业应用推荐的水平，并对应于食品或者饲料中草甘膦残留的低水平。三种人类细胞分别为新生儿脐带静脉的细胞、293 胚肾细胞与 JEG3 胎盘细胞系。所有草甘膦的配方在 24 小时内造成所有细胞死亡，通过抑制线粒体琥珀酸脱氢酶活性，以及通过释放胞质膜伤害腺苷酸激酶测量膜损伤导致坏疽。通过激活酶的半胱天冬酶 3/7 活性诱发细胞凋亡。单独草甘膦激起仅细胞凋亡，而人脐静脉内皮细胞（HUVEC）在这个水平上 100 倍更敏感。有害效应与草甘膦浓度不成比例，更加取决于除草剂辅佐剂的性质。草甘膦代谢物 AMPA 与 POEA（草甘膦除草剂配方中的表面活性剂），分别单独作用或者合在一起协作用时，像草甘膦一样，损伤细胞膜，但是各自在不同的浓度发挥作用。它们与草甘膦一起的混合物的危害通常更强。结论，像 POEA 这样的辅佐剂，改变人类细胞的渗透性，以凋亡与坏疽方式强化诱发草甘膦诱发的毒性。草甘膦真正的阈值，必须考虑存在的辅佐剂，还必须考虑草甘膦的代谢、时间放大效应或生物蓄积作用。市场上销售的草甘膦除草剂，即便在抗草甘膦作物加工的食品与饲料残留水平，能够造成细胞损伤以至死亡。

10) Nora Benachour and Gilles-Eric Séralini, Glyphosate Formulations Induce Apoptosis and Necrosis in Human Umbilical, Embryonic, and Placental Cells, *Chem. Res. Toxicol.*, 2009, 22 (1), pp 97–105

Nora Benachour and Gilles-Eric Séralini, 草甘膦配方除草剂在人类脐带、胚芽与胎盘细胞诱发凋亡与坏疽，化学研究毒理学，2009, 22 (1), pp 97–105

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**科学证据 11（2009）：**草甘膦为基础草甘膦在世界上最广泛使用。它们的残留成为环境中经常有的污染物。此外，这些除草剂还喷洒到最大量食用的转基因作物，这样的作物使其容忍细胞中高水平的这些成分。某些饲料中允许它们高达 400 ppm 残留。人类肝脏 HepG2 细胞是研究异型生物物质毒性的知名模型，我们让人类肝脏 HepG2 细胞接触草甘膦及其四种不同配方除草剂制剂。通常仅在慢性活体内对单独草甘膦成分进行试验。我们用三种试验方法（Alamar Blue, MTT, ToxiLight），以及基因毒性（彗星试验）、抗雌激素（对 ERalpha, ERbeta）与抗雄激素效果（对 AR）做基因检测试验。我们还用芳香化酶活性与 mRNA 检测雄激素雌激素转换。所有指标在 24 小时内都受到亚农业用剂量用的草甘膦及其四种配方除草剂制剂所有成分的干扰。其效果更依赖于草甘膦除草剂的配方而非草甘膦的剂量。首先观察到的人类细胞内分泌干扰是最为活性配方制剂（R400）从 0.5 ppm 剂量在 MDA-MB453-kb2 细胞中对雄激素受体的作用，然后从 2 ppm 剂量起，HepG2 细胞的两个雌激素受体的转录活动性遭到抑制。从 10 ppm 剂量起，芳香化酶转录和活动收到干扰。在 Alamar Blue 试验（最敏感的）中，从 10 ppm 剂量其发生细胞毒性作用，但从 5 ppm 起发生 DNA 损伤。因此必须考虑食物、饲料或者环境中草甘膦除草剂对真实细胞的影响，对草甘膦分类为致癌物/致突变/致生殖毒性进行了讨论。

11) Gasnier C, Dumont C, Benachour N, Clair E, Chagnon MC, Séralini GE. Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. Toxicology. 2009;262:184-91. doi:10.1016/j.tox.2009.06.006.  
Gasnier C, Dumont C, Benachour N, Clair E, Chagnon MC, Séralini GE。草甘膦除草剂在人类细胞系中致细胞毒性而且是内分泌干扰剂毒理学。  
2009;262:184-91.

<http://www.ncbi.nlm.nih.gov/pubmed/19539684>

**科学证据 12（2010）：**研究结果表明商业配方的草甘膦除草剂在体内是一种威力强大的内分泌干扰剂，青春期接触时对老鼠的生育系统发育造成干扰。

12) Romano RM et al., Prepubertal exposure to commercial formulation of the herbicide glyphosate alters testosterone levels and testicular morphology. Arch Toxicol. 2010 Apr;84(4):309-17. Epub 2009 Dec 12.

Romano RM et al., 青春期前接触商业草甘膦除草剂改变睾丸激素水平与睾丸形态。毒理学档案。2010 年 4 月； 84(4):309-17. 网络发表 2009 年 12 月 12 日。

就职机构：巴西 Sao Paulo 大学兽医学院，动物生殖与荷尔蒙实验室剂量系  
<http://www.ncbi.nlm.nih.gov/pubmed/20012598>

**科学证据 13 (2010):** 用 1ppm 浓度草甘膦对沙漏树蛙蝌蚪处理后，近 60% 发育失调。

13) Jayawardene, U.A et al., (2010). Toxicity of agrochemicals to common hourglass tree frog (*Polypedates crugiger*) in acute and chronic exposure. International Journal of Agriculture and Biology, 12, 641-648.

Jayawardene, U.A et al., (2010)。农业化学品急性与慢性接触对普遍的沙漏树蛙 (*Polypedates crugiger*) 的毒性。国际农业与生物学杂志， 12, 641-648.

[http://www.fspublishers.org/ijab/past-issues/IJABVOL\\_12\\_NO\\_5/1.pdf](http://www.fspublishers.org/ijab/past-issues/IJABVOL_12_NO_5/1.pdf)

**科学证据 14 (2010):** 非洲爪蟾蜍晶胚与稀释 5000 倍草甘膦除草剂一起孵化。经处理的晶胚高度异常，头盖与神经嵴明显改变，前后轴缩短。改变后神经嵴标记与颅软骨蝌蚪阶段畸形一致。注射单独草甘膦显示非常类似的畸形。草甘膦除草剂在鸡晶胚中显示类似的影响，显示一个逐渐失去了菱域。减少视觉囊泡和小头畸形。这表明草甘膦自己对观察到的畸形负责，而不是草甘膦除草剂配方中的表面活性剂或其他组分。一个报告基因分析，揭示草甘膦除草剂处理增加了非洲爪蟾蜍晶胚中的视黄酸活性，而且与 RA 拮抗剂的协作处理保持了草甘膦除草剂的致畸效应。因此结论草甘膦除草剂产生的显型主要是内源性类活动增加的结果。

14) Paganelli, A.et al., (2010). Glyphosate- based herbicides produce teratogenic effects on vertebrates by impairing retionic acid signaling. Chemical Research in Toxicology, 23, 1586-1595.

Paganelli, A.et al., (2010)。草甘膦基除草剂通过损伤损害视黄酸信号对脊椎动物造成畸形影响。毒理学化学研究, 23, 1586-1595.

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<http://pubs.acs.org/doi/abs/10.1021/tx1001749>

科学证据 15 (2012): 草甘膦除草剂是世界最大量销售的除草剂；最普遍的配方制剂农达含 POEA 作为其主要表面活性剂。最新的发现表明，暴露于草甘膦对人类可能造成 DNA 损伤与癌症。...与早期的草甘膦对内部器官淋巴与细胞的研究进行比较表明，上皮细胞更容易受到细胞毒性，而且 DNA 损伤的性质与除草剂及其配方相关。由于我们发现农业中喷洒剂量稀释 450 倍的短期暴露造成基因毒性的影响，我们的发现表明，喷洒草甘膦除草剂可能造成吸入人类 DNA 损伤。

15) Koller VJ, Furhacker M, Nersesyan A, Misik M, Eisenbauer M, Knasmueller S. Cytotoxic and DNA-damaging properties of glyphosate and Roundup in human-derived buccal epithelial cells. Arch Toxicol. 2012;86:805–813. doi:10.1007/s00204-012-0804-8.

Koller VJ, Furhacker M, Nersesyan A, Misik M, Eisenbauer M, Knasmueller S. 草甘膦与农达在人类口腔上皮细胞中造成细胞毒性与 DNA 损伤的性质。毒理学档案。2012;86:805–813.

<http://link.springer.com/article/10.1007%2Fs00204-012-0804-8>

科学证据 16 (2013) “该研究演示所试验的所有草甘膦为基础的除草剂都比单独草甘膦更为毒性.....配方除草剂（包括农达）可以影响所有活的细胞，特别人类细胞。在它们之中，（农达配方中的表面活性剂）POE-15 清楚显示是对人类细胞最为毒性的成分.....除了 POE-15 在它的首次胶束

化作用发生时诱发坏疽之外，这与草甘膦进入系背后促进内分泌干扰作用有所不同。”

16) R. Mesnagea, B. Bernayc, G.-E. Séralinia, Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity, *Toxicology*, Volume 313, Issues 2–3, 16 November 2013, Pages 122–128  
<http://www.sciencedirect.com/science/article/pii/S0300483X12003459>

科学证据 17 (2013)：草甘膦是最为广泛使用并被人们相信比其他农药毒性较低的除草剂的活性成分。然而，最近几项研究显示它对人类潜在危害健康，而且可能是一种内分泌干扰剂。该项研究集中于纯草甘膦对雌激素受体蛋白（**estrogen receptors**）促进的转录活动性及其表达。草甘膦，在  $10^{-12}$  至  $10^{-6}$  M (万亿分之一至百万分之一质量) 范围，在雌激素撤走状态下仅对人类激素-依赖乳房癌细胞 T47D 细胞发挥增殖作用，而对激素-独立乳房癌细胞 MDA-MB231 细胞系没有这种作用。诱发 ERE (雌激素反应元素) 转录活动性达到 T47D-KBluc 细胞中对照组的 5-13 倍的产生增殖作用剂量的草甘膦，受到一种雌激素对抗药 ICI 182780 的抑制，表明草甘膦的雌激素活性通过雌激素受体蛋白（**estrogen receptors**）发挥作用。此外，草甘膦既改变雌激素受体蛋白（**estrogen receptors**） $\alpha$ ，有改变其  $\beta$  表达。这些结果显示，在低的与环境性相关浓度下，草甘膦具有雌激素性活动。草甘膦为基础的除草剂广泛用于（转基因）大豆种植，而我们的结果发现，存在着草甘膦与大豆中的一种植物雌激素染料木黄酮（genistein）之间的额外雌激素作用。然而，草甘膦对于（转基因）大豆的这种额外的作用需要进行进一步的动物试验。

17) Thongprakaisang S, Thiantanawat A, Rangkadilok N, Suriyo T, Satayavivad J. Glyphosate induces human breast cancer cells growth via estrogen receptors. *Food Chem Toxicol.* 2013. doi:10.1016/j.fct.2013.05.057.

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